

Junction sequences of ChimeriVax™-JE (YF/JE) virus

Signalase

YAGA
MTGG
MTGG

MKL
VTL
MKL

Signalase

TNVHA
LGVGA
TNVGA

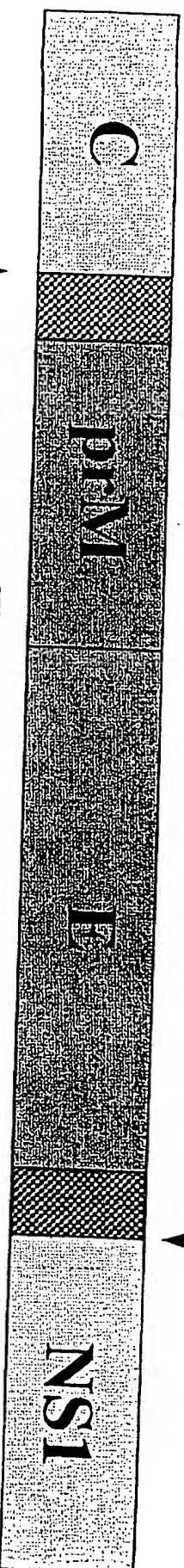
DTGCA
DQGCA
DQGCA

NS2B-3 protease*

NKR
KRR
KRR

GCNE
SHDV
SHDV

JE
YF
YF/JE



*: This cleavage is prerequisite for efficient signalase-mediated processing at the C/prM junction

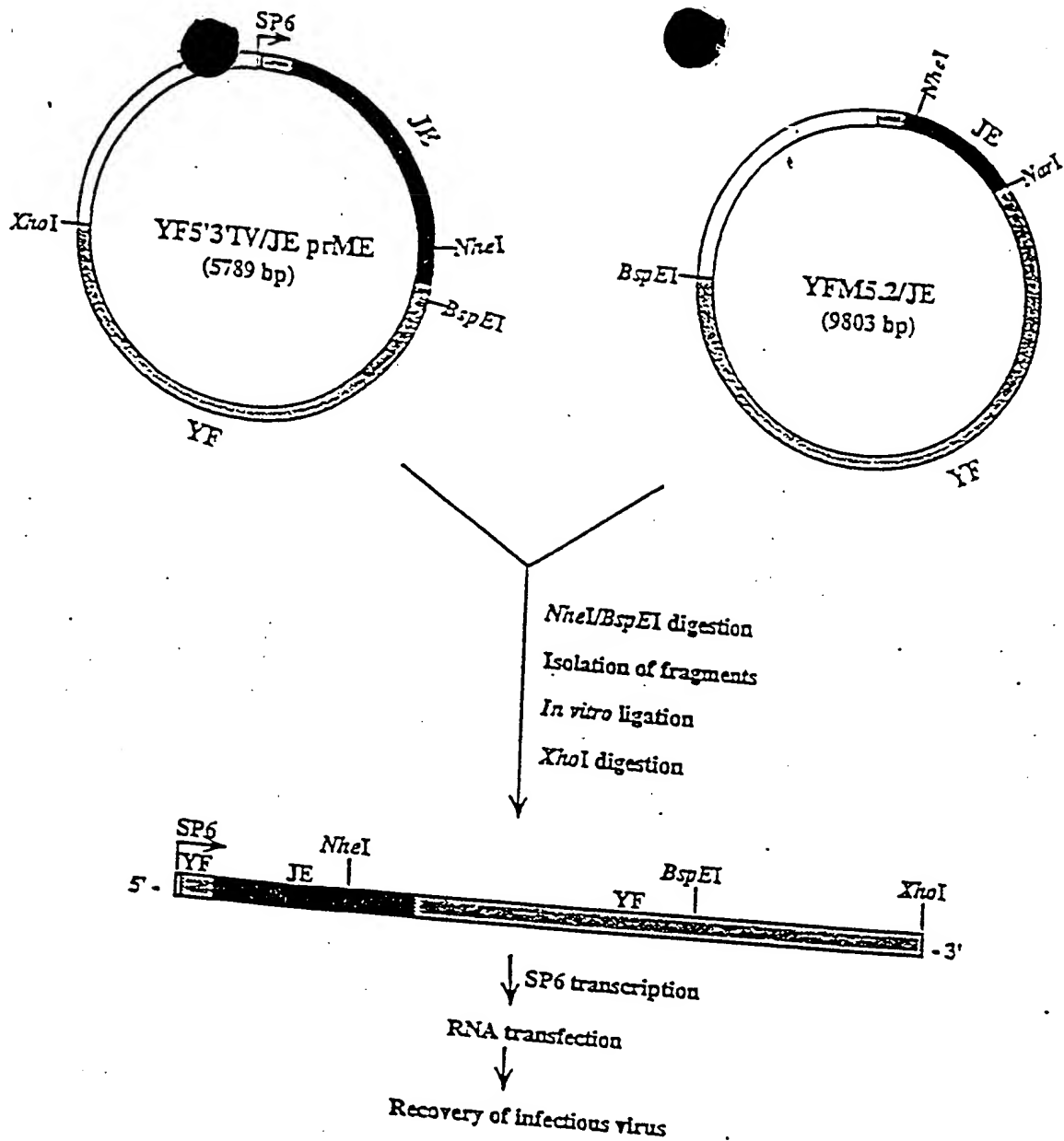


Fig. 2

05121537.072393

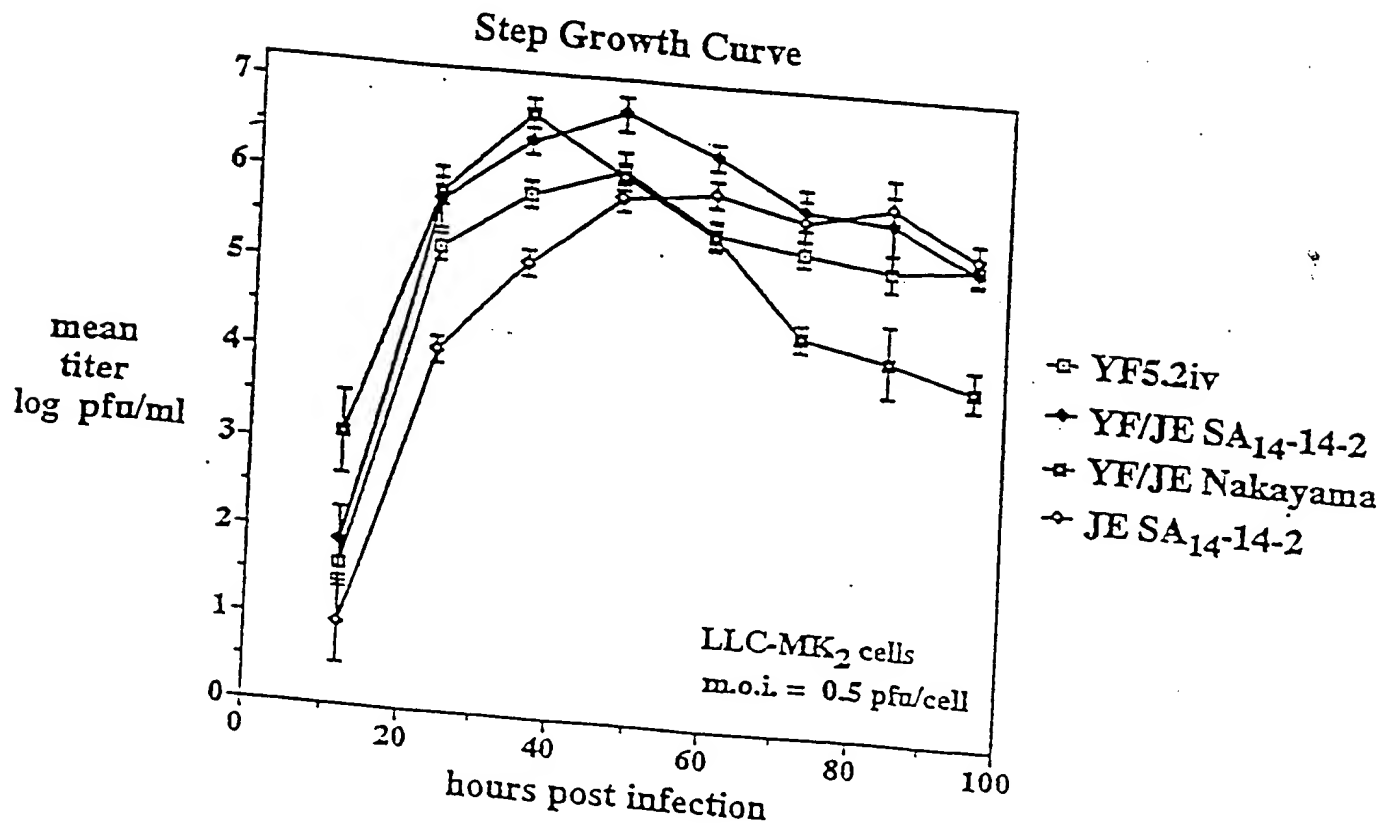
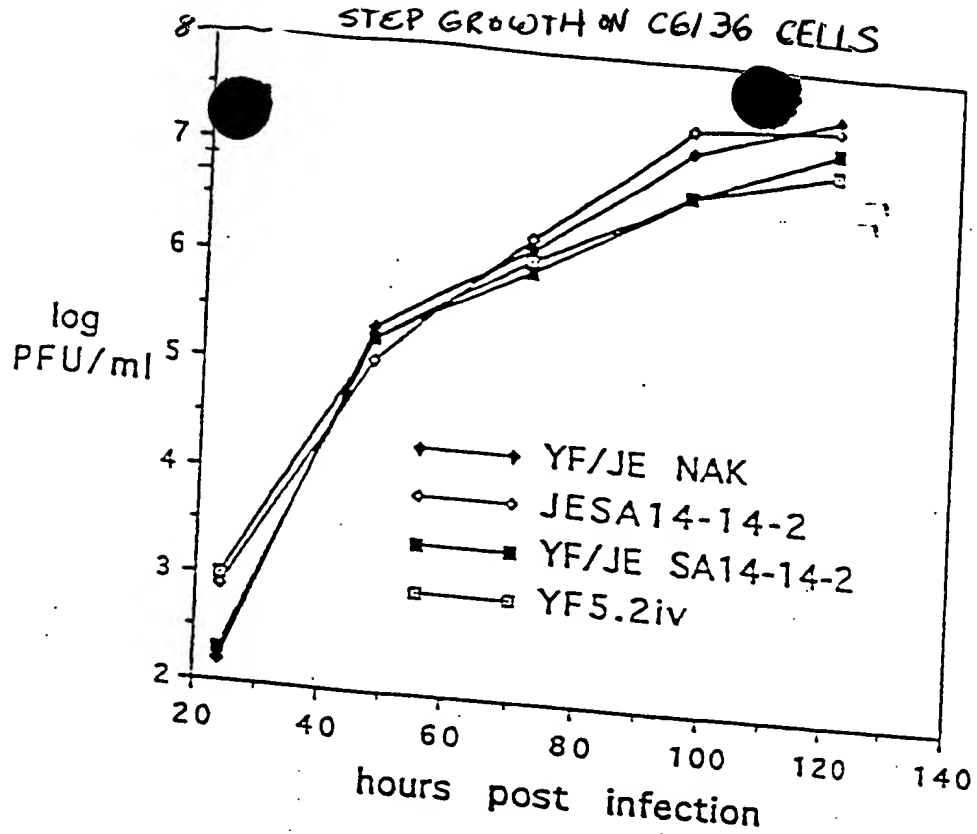


Fig 3

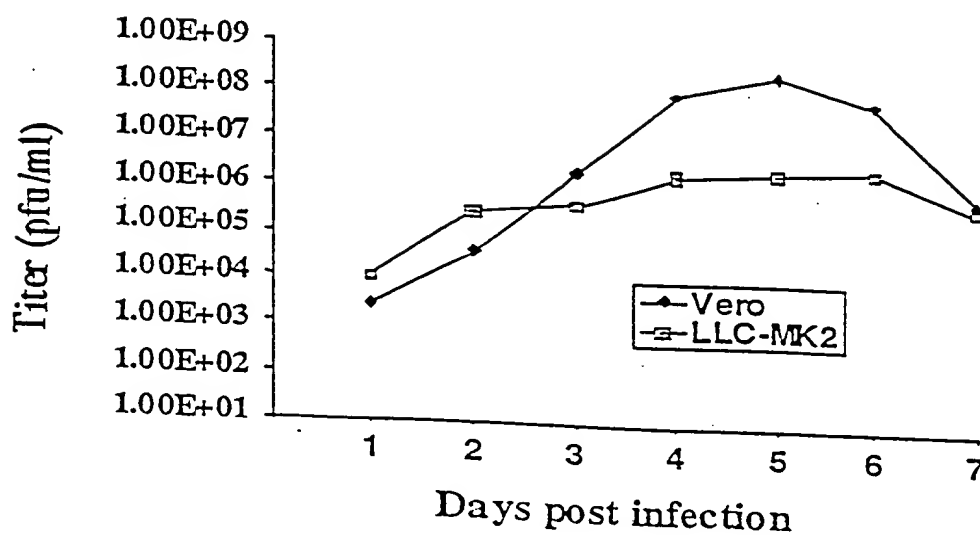
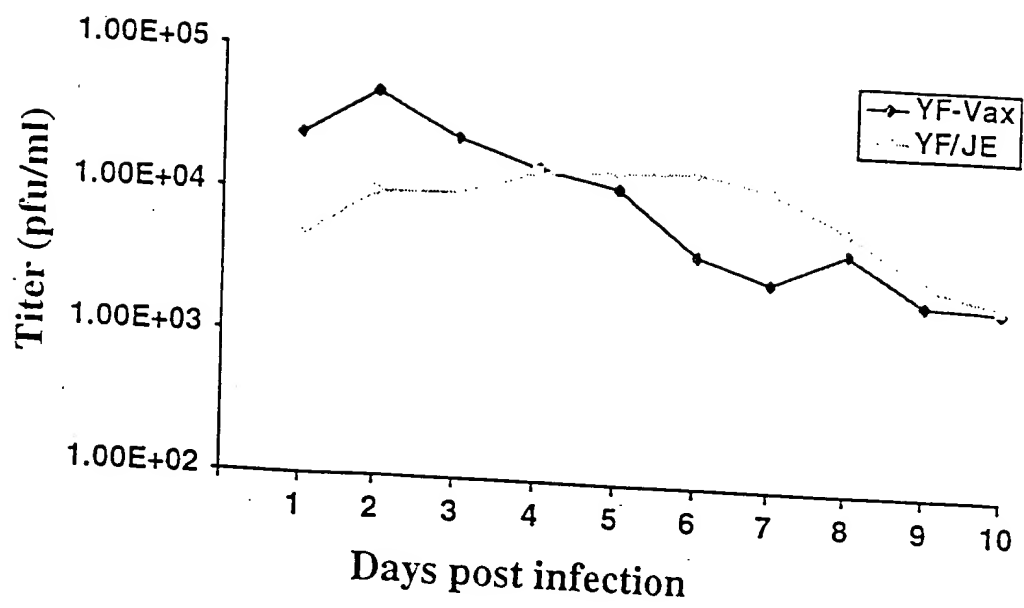


Fig. 4. Growth curves of RMS (YF/JE_{SA14-14-2}) in Vero and LLC-MK2 cells.

0914597-072358
362220-2857650



Growth comparison between RMS and YF-Vax in MRC-5 cells.

Fig.5

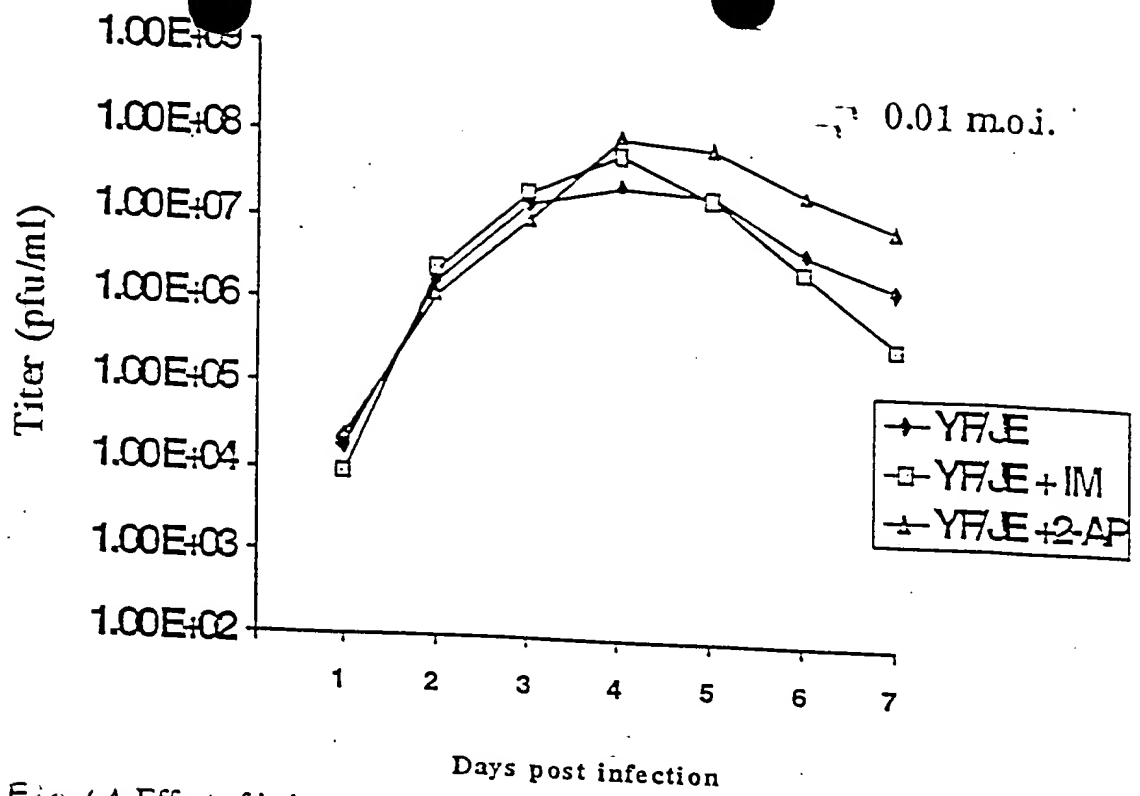


Fig. 6A, Effect of indomethacin (IM) or 2-aminopurine (2-AP) on growth kinetics of YF/JE (0.01 MOD) in FRhL cells

SA14-14-2

0011107-072398

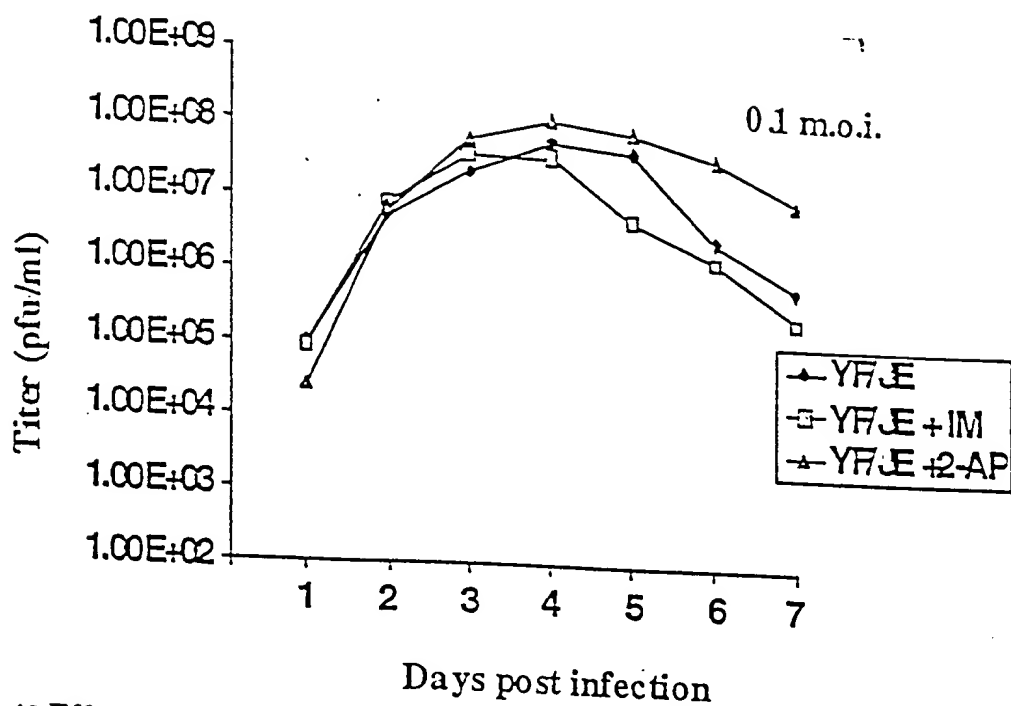
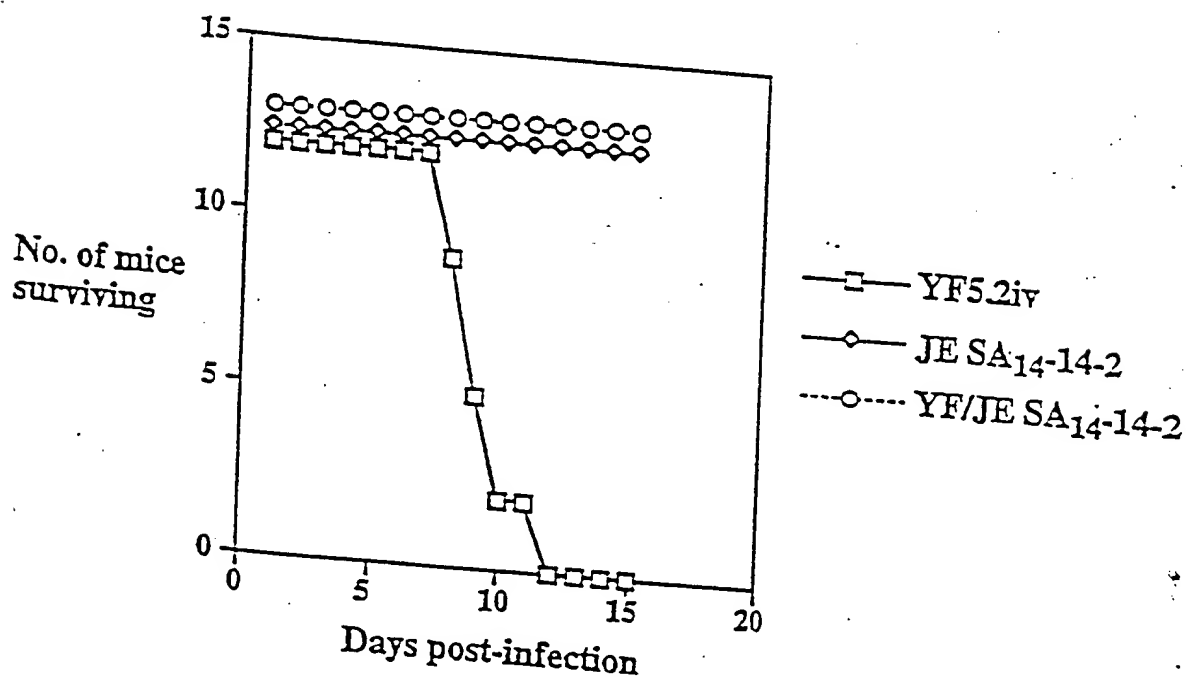


Fig. 62 Effect of indomethacin or 2-aminopurine on growth kinetics of YF/JE_{SA14-14-2} (0.1 MOI) in FRhL cells.

09121587.072398

Mouse neurovirulence analysis

MICE: 4 week old ICR males/females
 VIRUS DOSE: 10^4 pfu intracerebrally



| Virus | Survival | P |
|-----------------------------|--------------|--------|
| YF5.2iv | 0/12 (0%) | - |
| JE SA ₁₄₋₁₄₋₂ | 12/12 (100%) | <0.001 |
| YF/JE SA ₁₄₋₁₄₋₂ | 13/13 (100%) | <0.001 |

Fig. 7

00121507.072398

Neutralizing antibody response
to YF/JE SA14-14-2 chimeric vaccine
(3-week old mice immunized, samples for testing taken at 6 weeks)

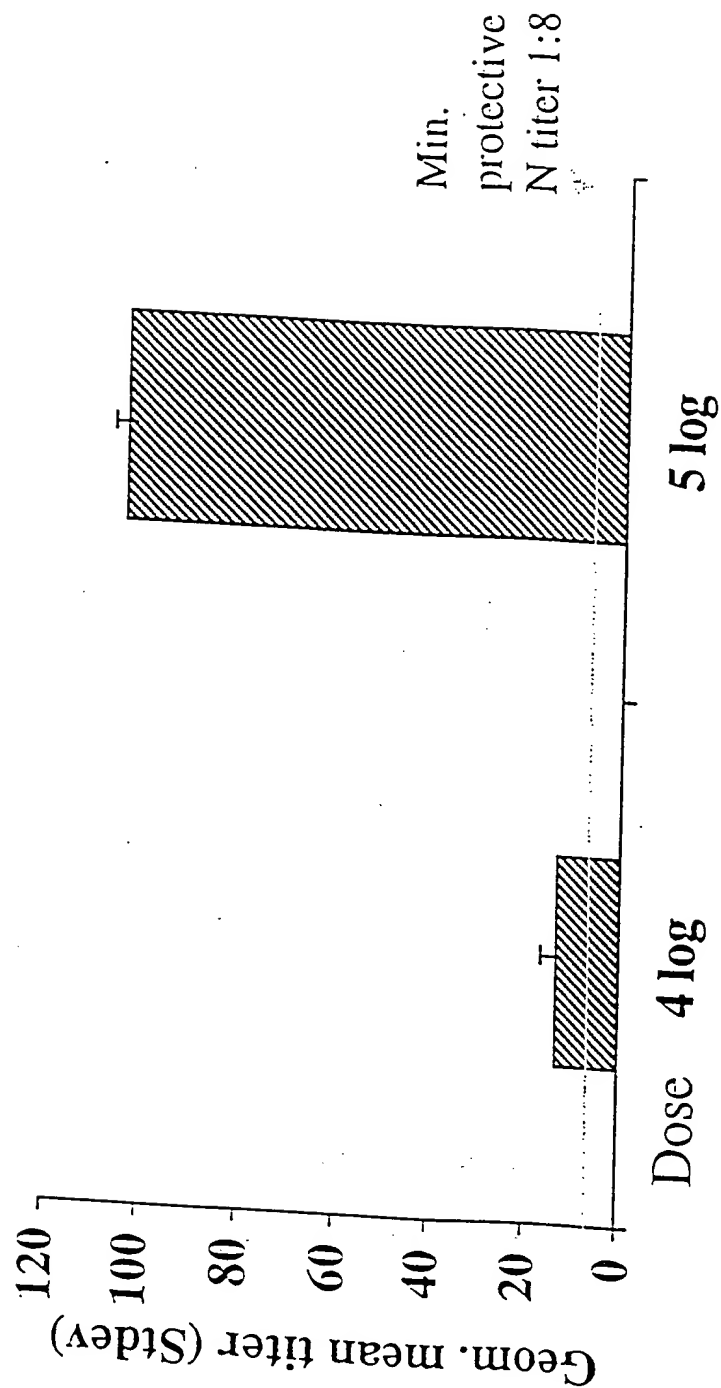


Fig. 8

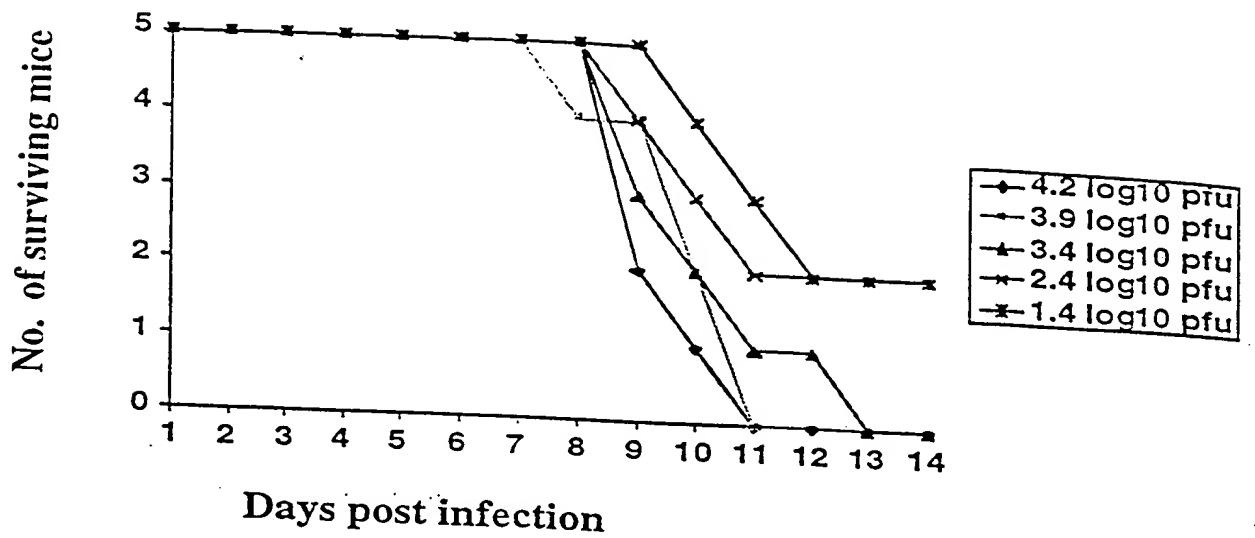


Fig. 9A. Neurovirulence testing of YF-Vax in 4-week old ICR mice by the i.c. route

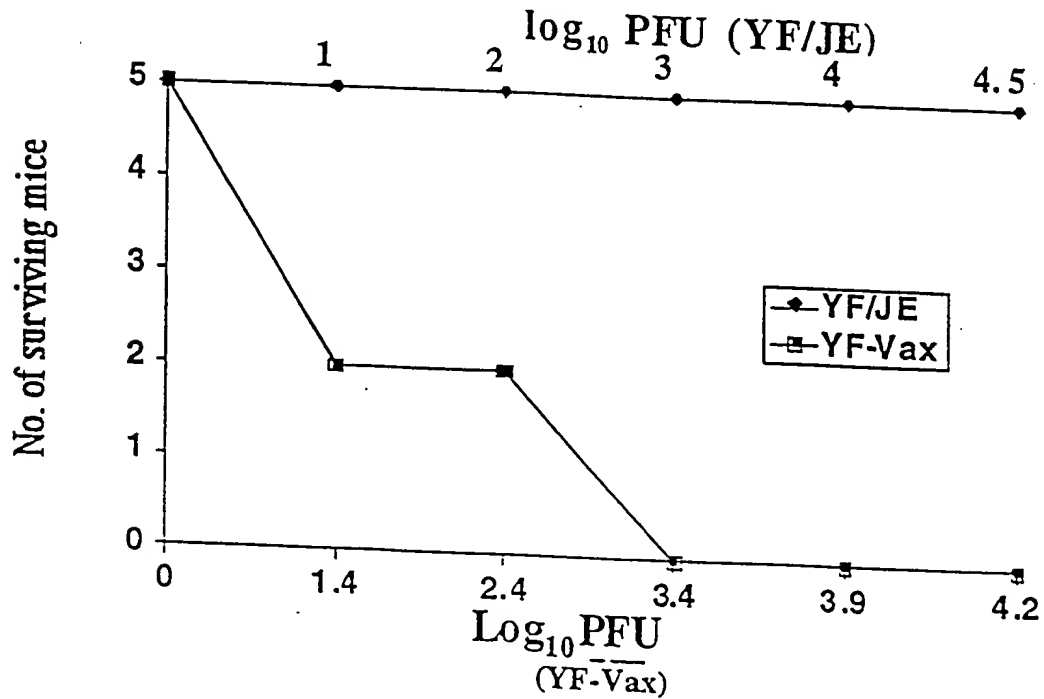


Fig. 9B. Neurovirulence testing of YF/JE_{SA14-14-2} in 4-week old ICR mice by I.C. route

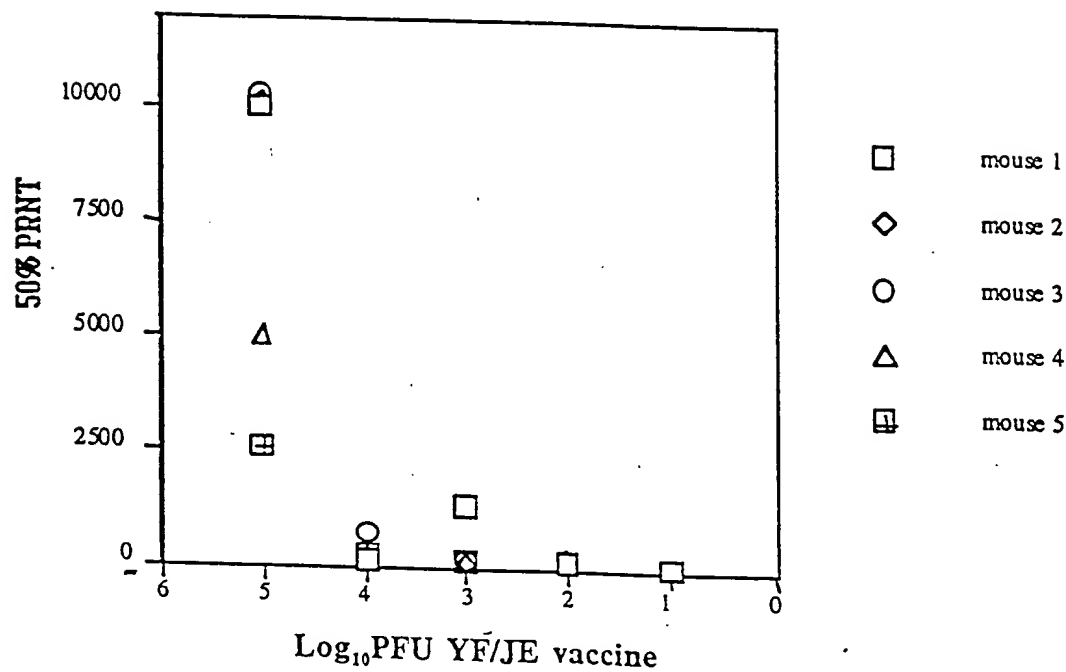
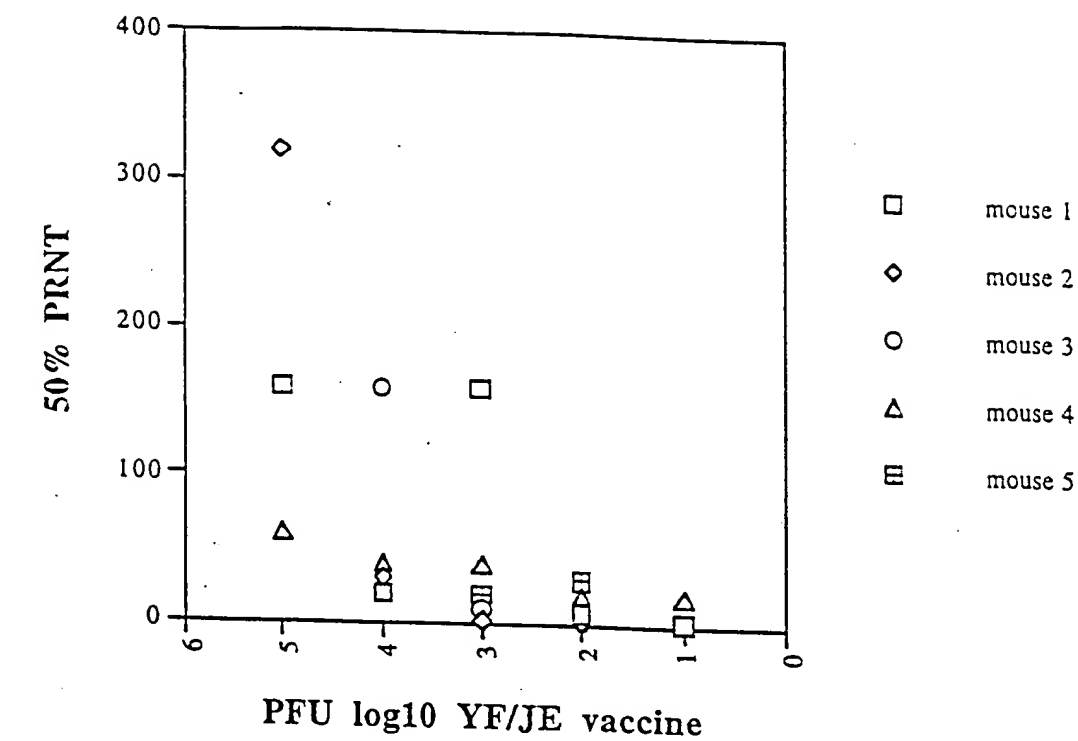


Fig. 10 Neutralizing antibody titers in mice inoculated s.c. with graded doses of YF/JE vaccine. TOP: 3 weeks post immunization and BOTTOM: 8 weeks post immunization

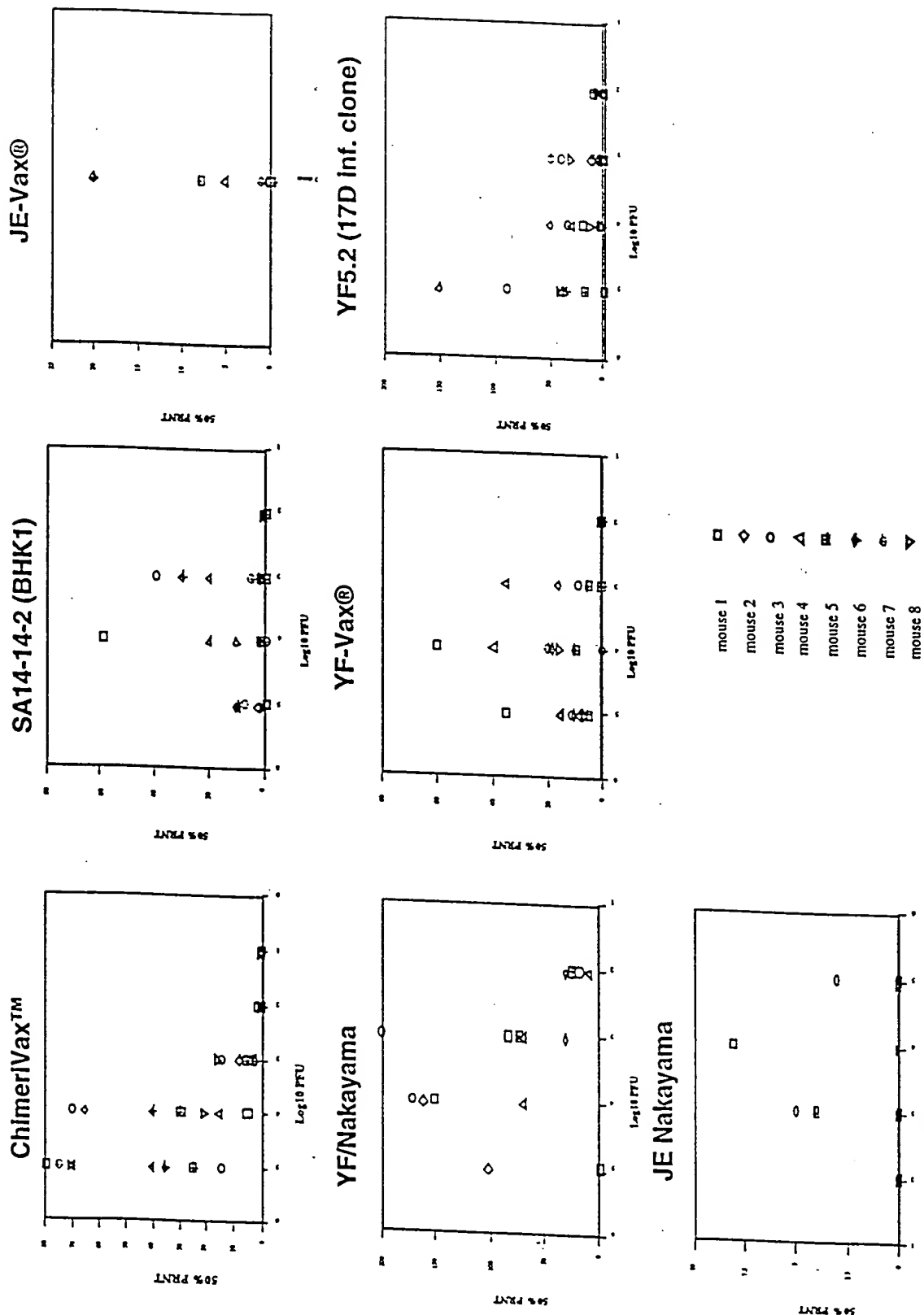


Fig. 1. SEROLOGICAL RESPONSES OF MICE IMMUNIZED WITH A SINGLE DOSE OF LIVE VIRUSES

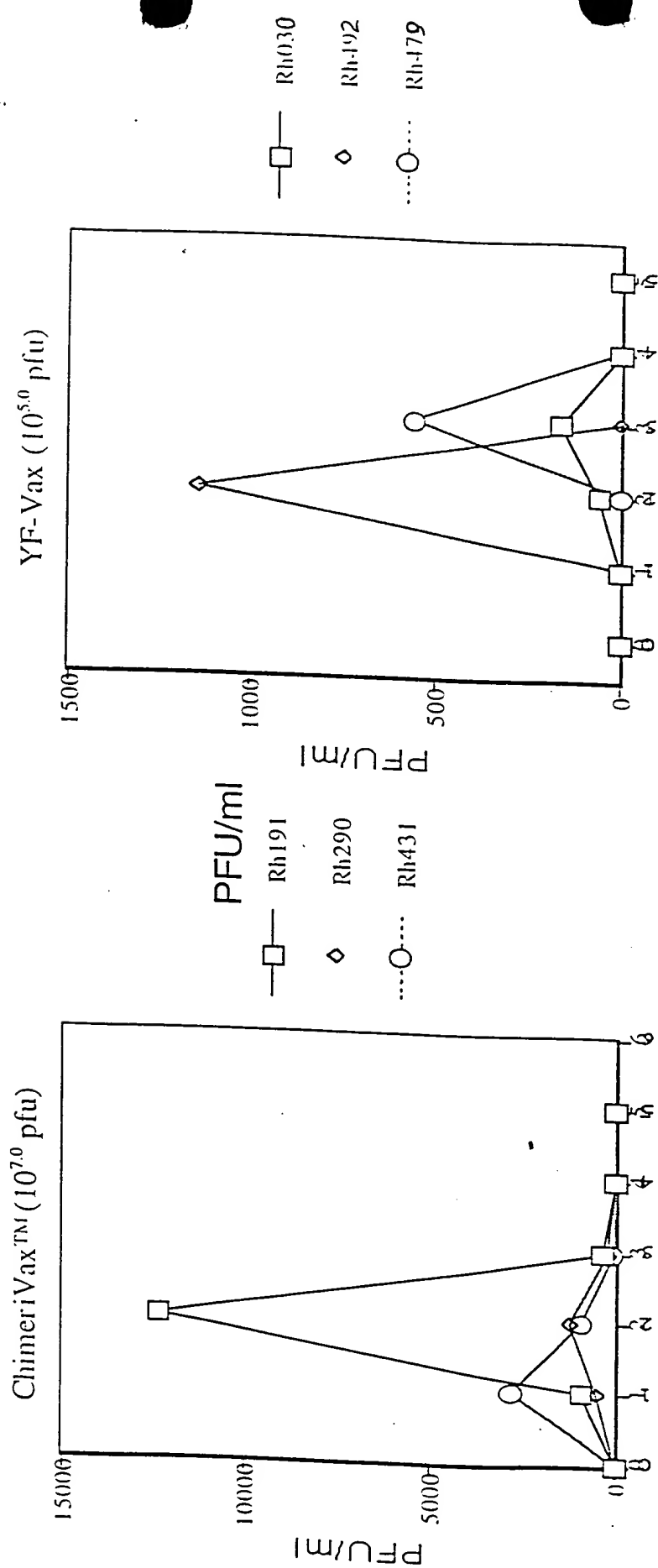


Fig. 12. Viremia and GMT of viremia in 3 rhesus monkeys inoculated with ChimeriVax™ or YF-Vax® by the I.C. route.

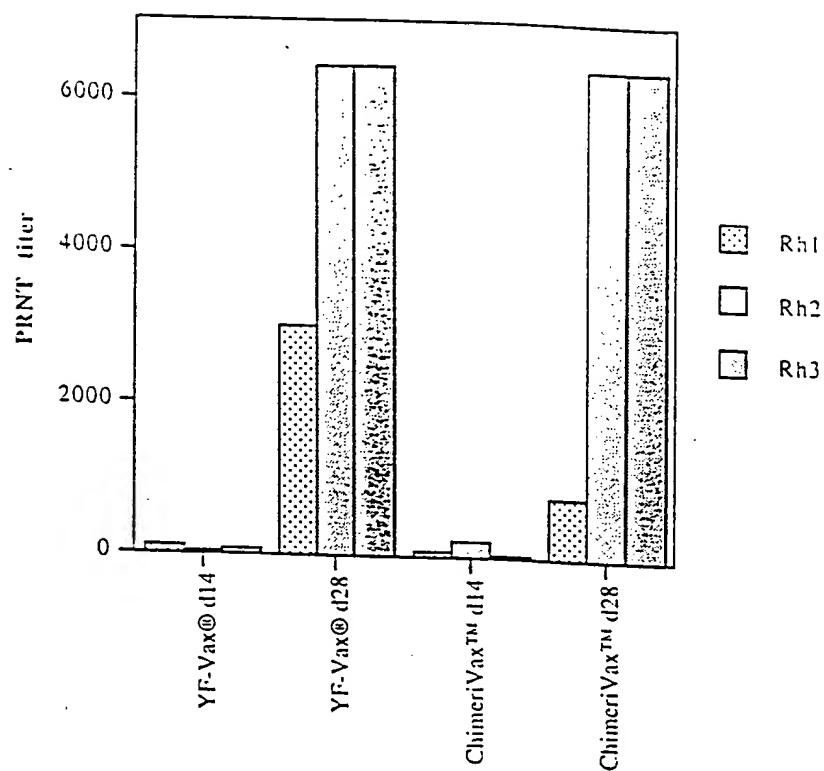


Fig. 13 Neutralizing antibody titers (50%) in rhesus monkeys 2 and 4 weeks post inoculations with a single dose of vaccines by the I.C. route.

The graph plots the number of surviving mice (Y-axis, 0 to 10) against days post-infection (X-axis, 1 to 14). Three data series are shown:

- YF/JE SA14-14-2 (E-138)** (diamonds): Survival remains high, starting at 10 and slightly decreasing to approximately 9.5 by day 14.
- YF/JE SA14-14-2** (squares): Survival remains stable at 8 mice from day 1 to day 7, then drops to 7 mice by day 8 and remains at 7 through day 14.
- YF/JE Nakayama** (triangles): Survival starts at 8 mice, remains stable until day 7, then drops sharply to 7 mice by day 8, 0.5 mice by day 9, and reaches 0 mice by day 10, remaining at 0 through day 14.

| Days post infection | YF/JE SA14-14-2 (E-138) | YF/JE SA14-14-2 | YF/JE Nakayama |
|---------------------|-------------------------|-----------------|----------------|
| 1 | 10 | 8 | 8 |
| 2 | 10 | 8 | 8 |
| 3 | 10 | 8 | 8 |
| 4 | 10 | 8 | 8 |
| 5 | 10 | 8 | 8 |
| 6 | 10 | 8 | 8 |
| 7 | 10 | 8 | 8 |
| 8 | 10 | 7 | 7 |
| 9 | 10 | 7 | 0.5 |
| 10 | 10 | 7 | 0 |
| 11 | 10 | 7 | 0 |
| 12 | 10 | 7 | 0 |
| 13 | 10 | 7 | 0 |
| 14 | 10 | 7 | 0 |

Fig. 14 Mouse neurovirulence testing of YF/JE SA14-14-2 (E-138 K-->E) mutant.

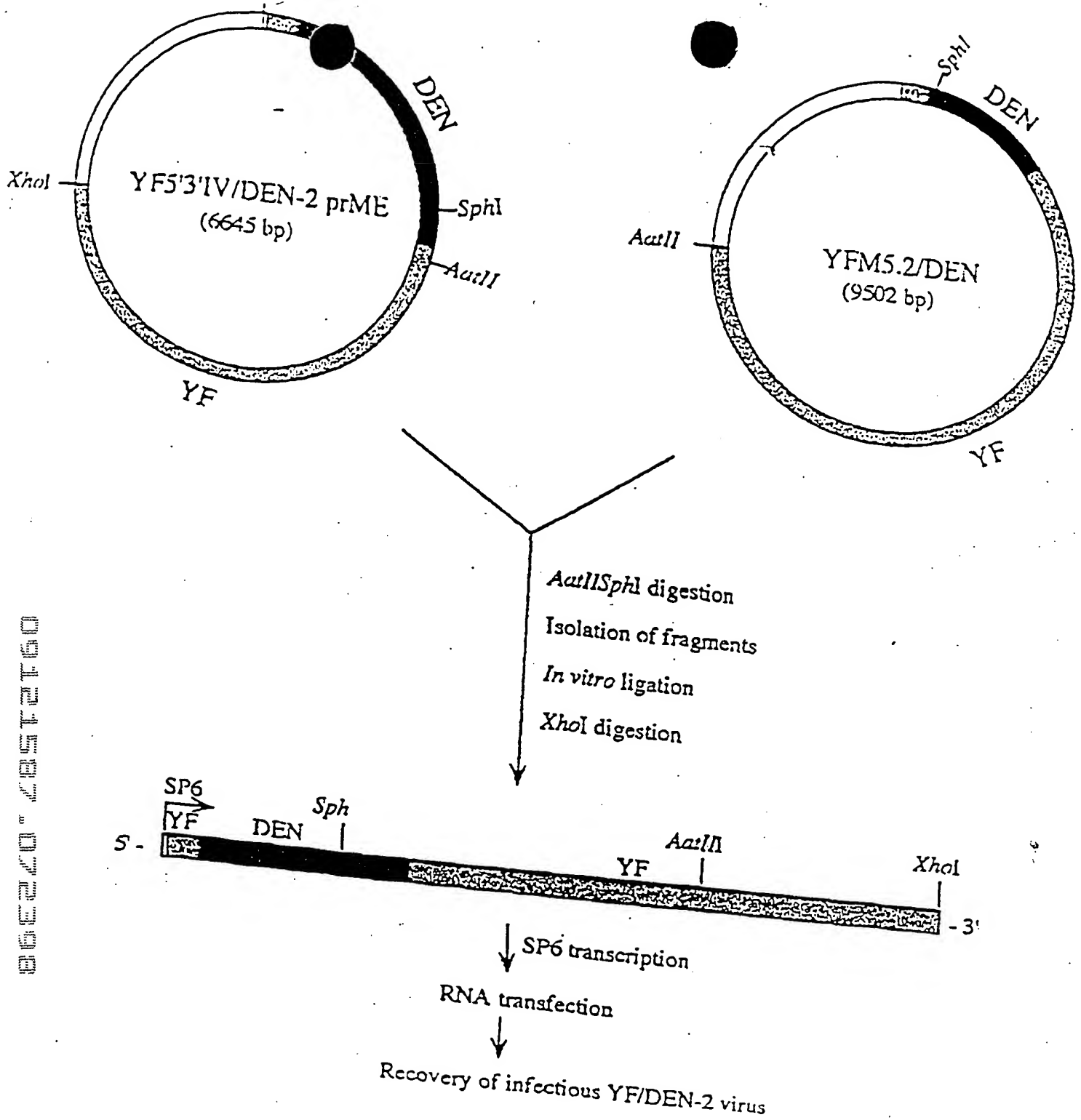


Fig. 15

Structure of modified YF clones expressing E/NS1 intergenic open reading frames

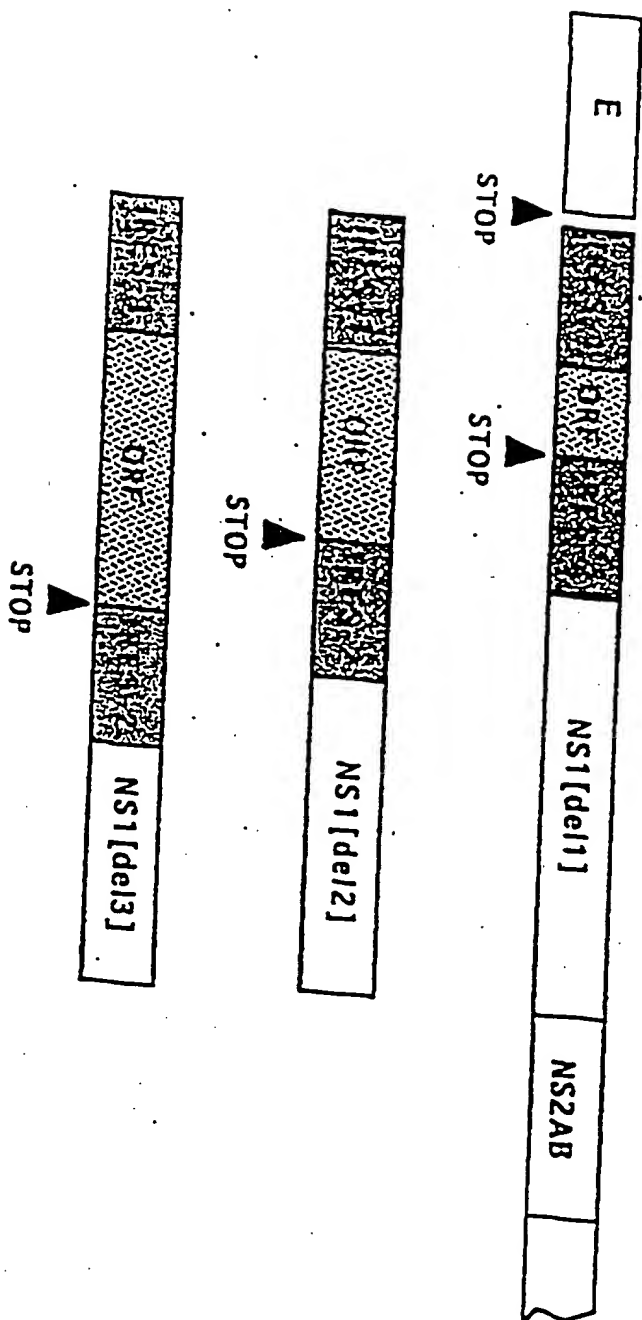


Fig. 16

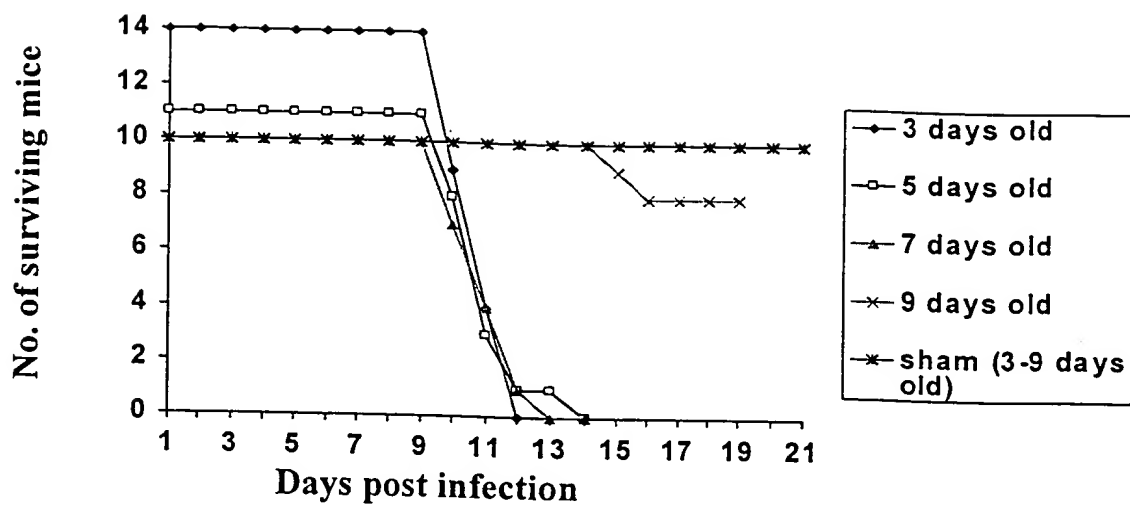


Figure 17. Neurovirulence phenotype of ChimeriVax™-Den2 in outbred (CD-1) suckling mice inoculated by the I.C. route with 10,000 PFU/0.02 ml.

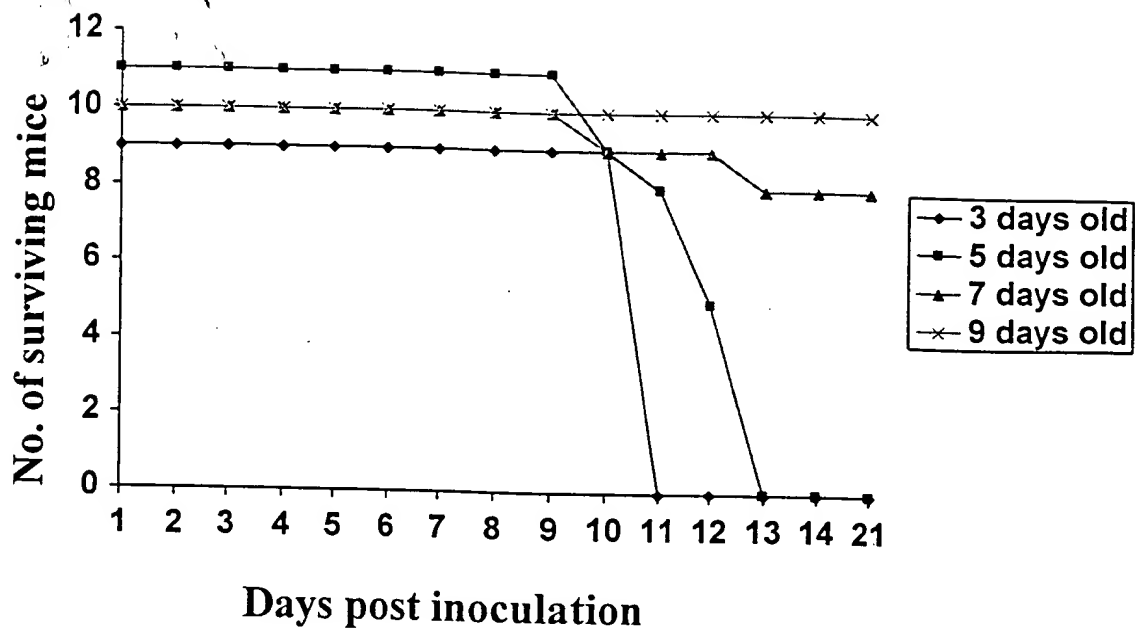


Figure 18. Neurovirulence phenotype of 17D vaccine (YF-Vax®) in outbred (CD-1) suckling mice inoculated by the I.P. route with 1000 PFU/0.02 ml.